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EXAMINER	
WILSON, MICHAEL C	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 04/07/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/757,054	PETITTE ET AL.	
	Examiner	Art Unit	
	Michael C. Wilson	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 January 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *44,47,48 and 51-55* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *44,47,48 and 51-55* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5-12-03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's arguments filed 1-2-04 have been fully considered but they are not persuasive. Claims 45, 46, 49, 50 have been cancelled. Claims 44, 47, 48 and 51-55 remain pending and under consideration in the instant office action. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC ' 112

1. Claims 44, 47, 48 and 51-55 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Regarding claims 44, 47 and 48, applicants' argue the specification taught combining PGCs and isolated at the same time as stromal cells and combining both with a preconditioned feeder matrix (pg 8, 1st ¶ of response). Applicants point to pg 3, line 19, through pg 4, line 2, and pg 8, lines 12-14. Pg 3 describes "collecting avian cells comprising primordial germ cells from an avian embryo after formation of the primitive streak; [and] (b) depositing the avian cells in contact with a preconditioned feeder matrix." Pg 8 describes, "avian gonadal cells comprising primordial germ cells isolated in accordance with the present invention also comprise a significant number of stromal cells."

Applicants argue isolating PGCs and stromal cells from an avian embryo after stage 14 has support on pg 10, lines 3-8 (pg 9 of response).

Applicants argue Example 2, pg 20, supports isolating PGCs and stromal cells and culturing them on feeder cells as claimed (pg 10, 3rd ¶ of response).

The new matter rejection regarding isolating PGCs and stromal cells at the same time from avian embryos and culturing those cells on a "preconditioned feeder matrix" (claim 44) has been withdrawn in part by applicants' arguments and in part by piecing together the specification.

The specification supports isolating PGCs and stromal cells from the gonad of an avian embryo together as claimed. Example 2, pg 20, line 10, explicitly describes culturing gonadal cells on STO feeder layers for 3-5 days (pg 10 of response). These "gonadal cells" (pg 20, line 10) implicitly refer to "gonadal PGCs and stromal cells" as claimed because they are collected from embryonic gonads and inherently have PGCs and stromal cells (pg 19, lines 14). The gonadal cells in Example 2 (pg 20, line 10) are generic to the gonadal cells comprising PGCs discussed on pg 8, lines 12-14.

The specification supports culturing gonadal cells with a "preconditioned" feeder matrix as claimed. The STO feeder cells in Example 2 were "preconditioned" prior to depositing of gonadal cells. Example 2 clearly states survival and proliferation of gonadal PGCs was affected by "preconditioning of the STO feeder layer" (pg 20, line 16), and "preconditioned" feeder matrix is defined as "cultured in the presence of media for a period of time prior to the depositing of gonadal cell comprising primordial germ

cells" (pg 11, lines 19-22). It is clear that the "feeder matrix" may be STO feeder cells or other feeder cells as described on pg 11, lines 11-16.

The specification supports isolating PGCs and stromal cells or avian feeder cells from avian embryos after Stage 14 (claims 44, 47 and 48). Example 2 implicitly supports isolating gonadal PGCs and stromal cells "from an avian embryo at a stage later than stage 14" because the cells were isolated at stage 27-30 (pg 19, line 15), and the application states the "[a]vian embryos from which cells are obtained for carrying out the present invention are preferably after stage 14" and "most preferably in stage 27-30" (pg 10, lines 3-8). It would have been readily apparent that any avian embryonic cells discussed in the specification, including avian feeder cells isolated from an avian embryonic gonad discussed on pg 11, lines 13-15, could have been isolated from an avian embryo after stage 14 as claimed (claim 47 and 48).

Claims 47 and 48 have support for "preconditioned" avian feeder cells (pg 11, line 13-15) because the specification taught "feeder matrix" included avian feeder cells isolated from the gonad (pg 11, lines 13-15) and that the "feeder matrix" can be "preconditioned" which meant "the feeder matrix is cultured in the presence of media for a period of time prior to the depositing of gonadal cell comprising primordial germ cells" (pg 11, lines 19-22). In context of Example 2, it would have been readily apparent to one of skill in the art that the "preconditioned" STO feeder cells on pg 20 in Example 2 could have been replaced with "preconditioned" avian feeder cells isolated from an avian embryonic gonad.

Claims 53 and 54 remain new matter. Applicants point to pg 13, line 21, through pg 14, line 7 (pg 14-15 of response). Applicants' argument is not persuasive. The specification teaches, "it is currently preferred to have a preconditioned feeder matrix to facilitate the survival and development of avian PGCs into undifferentiated avian cells expressing an ESC phenotype. The avian embryo cells of the present invention can be cultured for at least one or two months." (pg 14, lines 1-5). While the specification taught PGCs were cultured to facilitate the survival and development of avian PGCs into "undifferentiated avian cells expressing an ESC phenotype," the specification did not teach or suggest the "undifferentiated avian cells expressing an ESC phenotype" were maintained for one or two months or that the "ESC phenotype" was maintained for one or two months as claimed. As written, the specification merely states the PGCs are maintained for one or two months. The specification did not teach or suggest that cells having an ES cell phenotype were maintained in culture for one to two months as claimed. The specification did not teach or suggest the ES cell phenotype was maintained in culture for one to two months.

2. Claims 44, 47, 48 and 51-55 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a culture comprising PGCs and avian feeder cells does not reasonably provide enablement for culturing PGCs and avian feeder cells for one or two months. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly

connected, to make and/or use the invention commensurate in scope with these claims for reasons of record.

Claims 53 and 54 require culturing the PGCs for more than a month or two months. At the time of filing, Ponce De Leon (1997, Revista Brasileira de Reproducao Animal, Vol. 21, pg 96-101) taught LIF, bFGF, IGF and SCF are required for long-term culture of avian PGCs (pg 100, col. 2, about half way down). However, the art did not teach how to culture avian PGCs in the presence of avian feeder cells for one or two months. The specification taught culturing avian PGCs on "preconditioned" STO feeder cells (Examples 1-3). The specification does not teach the amounts of essential growth factors that were required to culture avian PGCs in the presence of feeder cells for one or two months. Given the teachings in the specification taken with the guidance provided in the specification, it would require one of skill in the art undue experimentation to determine how to maintain avian PGCs in the presence of avian feeder cells for one or two months.

The specification does not enable obtaining culturing PGCs having an ES cell phenotype for at least one or two months as broadly claimed. An ES cell is considered a cell capable of becoming both a somatic and germ cell upon being introduced into an embryo (pg 1, line 17). Simkiss (1990, 4th World Congr. Genetic Appl. Livestock Prod., Vol. 16, pg 111-114) and Petitte (1990, Development, Vol. 108, pg 185-195) taught chicken PGCs capable of producing somatic and germ cell chimeric chickens. The stage of isolation and culture conditions required to maintain chicken ES cells for at least a month or two are not taught in the art or the specification. The stage and

conditions required to obtain ES cells in species other than chickens are not taught in the art or the specification. Given the teachings in the art taken with the teachings in the specification, it would have required one of skill undue experimentation to isolate any avian ES cell other than chicken ES cells or to maintain any ES cell for one or two months as broadly claimed.

Applicants argue Ponce de Leon does not disclose the conditions of LIF, bFGF, IGF and SCF that did provide long term culture of PGCs. Therefore, applicants conclude it is not possible to determine what LIF, bFGF, IGF and SCF conditions were necessary to sustain culture for one or two months. Applicants' argument is not persuasive. Claims 54 and 55 do not require LIF, bFGF, IGF or SCF, which is considered essential to sustain the culture according to Ponce de Leon. While Ponce de Leon did not teach the amounts of each growth factor used, Ponce de Leon need not be fully enabling to establish that these growth factors were essential to sustaining PGC cultures as claimed and that the amount of growth factors required to sustain PGCs for one or two months as claimed was unknown. Ponce de Leon need not teach the amounts of growth factors used to sustain PGC cultures to establish the state of the art at the time of filing.

Applicants point to Examples 1-3 and state various numbers of PGCs grown on various numbers of STO feeder cells enables the invention (pg 16 of response). Applicants' argument is not persuasive because the specification does not teach the essential amounts of growth factors required to sustain PGCs for one or two months as claimed and the amounts were not taught in the art.

Applicants argue the specification enables culturing any avian cell as broadly claimed (pg 17). Applicants point out that the specification describes the appropriate stage as after stage 14, or after formation of the primitive streak. Applicants' argument is not persuasive. Different avians have different stages and the culture conditions required to culture PGCs isolated from different avian species varies. The specification is silent regarding the differences between the stages of chickens and other avians. The specification is silent regarding the differences between the culture conditions for chicken PGCs and other avian PGCs.

Applicants' arguments regarding Bosselman are moot (pg 18, 1st ¶). The claims do not require transformed avian embryonic cells.

In view of the dearth of information in the art at the time of filing required for one of skill to isolate any avian ES cell other than chicken ES cells or to maintain any ES cell for one or two months as claimed, the parameters required to obtain such a result are essential to the invention. Because the specification does not teach the essential elements required to obtain results not known in the art, the amount of experimentation required by one of skill to obtain such results is, by its very nature, undue. Examples 1, 2 and 3 merely reiterate parameters known in the art. Pg 4, line 18-20, pg 8, lines 20-22 and pg 12, lines 4-8, merely list avian species. The teachings cited do not overcome the unpredictability in the art by providing the specific conditions required to isolate any avian ES cell other than chicken ES cells or to maintain any ES cell for one or two months as broadly claimed. The conditions described in the specification are not "a reasonable amount of guidance" because they are not distinguishable from conditions

known in the art. The conditions described in the specification are not adequate for one of skill to determine the parameters required to obtain results not known in the art. Therefore, it would have required one of skill undue experimentation to isolate any avian ES cell other than chicken ES cells or to maintain any ES cell for one or two months as claimed.

3. Claims 44, 47, 48 and 51-55 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for reasons of record.

The cells encompassed by the phrase "undifferentiated avian cells expressing an embryonic stem cell phenotype" are unclear (claim 44). It is unclear if the cells merely share a phenotype in common with avian ES cells or if the cells are avian ES cells capable of making germline chimeras upon being introduced into a recipient embryo. The specification states, "embryonic stem cell phenotype refers to undifferentiated avian cells having a large nucleus, prominent nucleolus and little cytoplasm" (pg 9, lines 4-5). Such a description is ambiguous because it cannot be determined what applicants consider "large," "prominent" or "little." The phrase "refers to" on pg 9, line 4, makes the citation unclear because it cannot be determined if "refers to" is intended to define the phenotype or merely to describing to what the phenotype is relevant. Therefore, it is unclear if "undifferentiated avian cells having a large nucleus, a prominent nucleolus, and little cytoplasm" is the "embryonic stem cell phenotype" or a description of a feature of an "embryonic stem cell phenotype." Ergo, it is unclear if "avian cells expressing an

ES cell phenotype" are defined as any "undifferentiated avian cells having a large nucleus, a prominent nucleolus, and little cytoplasm" or if "avian cells expressing an ES cell phenotype" have to do with (are relevant to) "undifferentiated avian cells having a large nucleus, a prominent nucleolus, and little cytoplasm." The specification also states an "'undifferentiated avian cell expressing an embryonic stem cell phenotype' encompasses cells derived from avian primordial germ cells and is therefore used to describe the cells cultured in accordance with the process of the present invention" (pg 9, lines 19-22). It is unclear if pg 9, lines 19-22, is the definition of "avian cells expressing an ES cell phenotype." The scope of cells encompassed by the description on pg 9, lines 4-5, is different than the scope of the cells encompassed by the description on pg 9, lines 19-22. One of skill would not be able to determine whether to use pg 9, lines 4-5, or pg 9, lines 19-22, as the definition of "avian cells expressing an ES cell phenotype" as claimed. In fact, one of skill would not have been able to determine that either citation was a definition of "avian cells expressing an ES cell phenotype" and not merely a description of features shared by "avian cells expressing an ES cell phenotype." Furthermore cells do not "express" a phenotype as on pg 9, line 19. Pg 1, line 17, states ES cell were capable of making germline chimeras. The phrase "embryonic stem cell phenotype" is mentioned on pg 3, lines 4-5, but does not clarify the meaning. One of skill in the art at the time of filing would have been unclear as to whether the specification was redefining ES cells or refining the art recognized meaning of ES cells as embryonic stem cells capable of making germline chimeras

upon being introduced into a recipient embryo. Therefore, the metes and bounds of cells encompassed by the phrase cannot be determined.

Applicants point to pg 9, lines 4-5, which has been addressed above (pg 19 of response).

Applicants' arguments' regarding US Patents (pg 19, last 8 lines) are moot because of the ambiguous teachings in the instant specification.

The rejection regarding "preconditioned feeder matrix" and "conditioned media" has been withdrawn in view of applicants' arguments and the definition of "conditioned media." The phrase "preconditioned feeder matrix" is defined on pg 11, line 20, as being a feeder matrix cultured in the presence of media for a period of time prior to the depositing of gonadal cells comprising primordial germ cells in contact with the feeder matrix." The phrase "conditioned media" refers to any media that has biologically active components obtained from previously cultured cells that have released into the media substances that affect cell function (see definition from On-line Medical Dictionary, attached). "Conditioned media" is not limited to media removed and transferred to other cells as described by applicants on pg 20, last lines. The media used to culture the "preconditioned feeder matrix" may also be considered "conditioned media" because it has previously cultured cells and has biologically active components released by the cells.

It remains unclear how PGCs isolated from an embryo later than stage 14 are distinguished from PGCs isolated from a stage X or stage 14 embryo (claim 44, 47, 48). PGCs isolated from stage X, 14 and after stage 14 embryos have the same structure

and function. As such, the structural/functional distinction of PGCs isolated after stage XIV as claimed cannot be determined. Applicants' discussion of PGCs isolated after stage 14 (¶ bridging pg 21-22 of the response) does not distinguish the structural and functional differences between PGCs isolated from stage X and XIV embryos.

Claim Rejections - 35 USC ' 102

The rejection regarding claims 44, 47, 48, 51-55 under 35 U.S.C. 102(b) as being anticipated by Allioli (1994, Devel. Biol., Vol. 165, pg 30-37) has been withdrawn because Allioli did not teach a "preconditioned feeder layer" (pg 23, last 3 lines, in the response), i.e. Allioli did not teach a feeder matrix cultured in the presence of media for a period of time prior to the depositing of gonadal cells comprising primordial germ cells in contact with the feeder matrix.

The rejection regarding claims 44, 47, 48 and 52-55 under 35 U.S.C. 102(e) as being anticipated by Ponce de Leon (US Patent 6,156,569) has been withdrawn. Cells isolated from the dorsal aorta of stage XIV embryos as taught by Ponce de Leon are not the same as avian primordial germ cells and avian stromal cells isolated from the genital ridge or gonad as claimed.

4. Claims 44, 47, 48, 52-55 remain rejected under 35 U.S.C. 102(b) as being anticipated by Chang (1995, Cell Biol. Internatl. Vol. 19. No. 2, pg 143-149) for reasons of record.

Chang taught making a feeder cells by isolating cells from the genital ridge of day 5 embryos and culturing the cells for 4 days (pg 143, "Preparation of germinal ridge and culture of stroma cells"). The feeder cells are "preconditioned" because they are in culture for 4 days prior to the addition of day-2 PGCs. The feeder cell media is "conditioned" because it contains biologically active components obtained from the previous 4 days in culture prior to adding day-2 PGCs. The cells isolated from the genital ridge comprised stromal cells and PGCs as claimed (pg 144, line 6). Day 5 embryos are greater than stage 14 as claimed because day 2 embryos are stage 14 (pg 144, col. 2, lines 1-10). Claim 51 has been withdrawn from the rejection because Chang did not teach using BRL conditioned media. The conditioned media taught by Chang had LIF, IGF and FGF-b (pg 144, col. 1, 1st full ¶). A PGC culture maintained for one or two months as claimed (claims 53, 54) does not differ from PGC cultures known in the art because their structure and functions are equivalent and because culturing PGCs for one or two months does not alter the structure or function of the culture. Therefore, the limitations in claims 53 and 54 do not bear patentable weight in considering the art because they does not distinguish the structure or function of the cells within the culture or the components of the culture from those known in the art.

Thus, Chang taught all the limitations of the claims.

Applicants argue Chang did not teach a "preconditioned feeder layer" or "conditioned medium" (pg 24, last full ¶). Applicants' arguments are not persuasive for reasons above.

5. Claims 44, 47, 48 and 52-55 remain rejected under 35 U.S.C. 102(b) as being anticipated by Chang (1997, Cell Biol. Internatl., Vol. 21, No. 8, pg 495-499) for reasons of record.

Chang taught isolating genital ridge stromal cells from day 5 (stage 27-28) embryos. The cells were cultured for 5 days in media containing IGF, FGF and LIF with germinal ridge stromal feeder cells isolated from day 5 embryos. gPGCs obtained from the culture were injected into recipient embryos and provided germline transmission (pg 496, "Preparation and culture of gPGCs"; pg 497, Fig. 1, "Progeny of germline chimeric chickens").

The "primary cultured GRSCs" (last sentence of "Preparation and culture of gPGCs") are a "preconditioned feeder matrix" because they were in culture prior to the addition of other GRSCs. The media of the "primary cultured GRSCs" was "conditioned" because it contained biologically active components obtained from the previous days in culture prior to adding other GRSCs. The cells isolated from the genital ridge and added to the "primary cultured GRSC" feeder cells inherently comprised stromal cells and PGCs. Day 5 embryos are stage 27 (pg 496, "Preparation and culture of gPGCs", line 2). Claim 51 has been withdrawn from the rejection because Chang did not teach using BRL conditioned media. The conditioned media taught by Chang had LIF, IGF and FGF-b (pg 496, "Preparation and culture of gPGCs"). A PGC culture maintained for one or two months as claimed (claims 53, 54) does not differ from PGC cultures known in the art because their structure and functions are equivalent and because culturing PGCs for one or two months does not alter the

structure or function of the culture. Therefore, the limitations in claims 53 and 54 do not bear patentable weight in considering the art because they does not distinguish the structure or function of the cells within the culture or the components of the culture from those known in the art.

Applicants argue Chang did not teach "conditioned medium" (pg 25, last full ¶). Applicants' argument is not persuasive for reasons cited above.

6. Claims 44, 47, 48 and 51-55 remain rejected under 35 U.S.C. 102(e) as being anticipated by Petitte (US Patent 5,340,740), Petitte (US Patent 5,656,479) or Petitte (US Patent 5,830,510) for reasons of record.

Petitte taught isolating and dissociating whole stage X chicken embryos, seeding the cells onto a preconditioned feeder layer, culturing the cells with BRL conditioned medium and obtaining PGCs (col. 7, lines 7-14, of '740; col. 6, line 44, of '479; col. 6, line 54-65, of '510). The PGCs and stromal cells were inherently "isolated together from the embryonic genital ridge or gonad" as claimed because the whole embryo was isolated and inherently contained both PGCs and stromal cells in the genital ridge or gonad. The PGCs and stromal cells in the whole dissociated embryo taught by Petitte are equivalent to PGCs and stromal cells isolated from the embryonic genital ridge or gonad as claimed because they have the same structure and function. PGCs and stromal cells from the stage X taught by Petitte are equivalent to PGCs and stromal cells isolated from an embryo later than stage 14 as claimed because they have the same structure and function.

Applicants argue the cells of Petitte are not isolated from an embryo later than stage 14. Applicants' argument is not persuasive. The structure and function of cells isolated from stage X as described by Petitte are the same as those of cells isolated from stage 14 as claimed.

Double Patenting

The rejection of claims 44, 47, 48 and 51-55 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 2, 3, 13, 19 and 23 of copending Application No. 08/446,021 (now US Patent 6,515,199) has been withdrawn because the claims of '199 are limited to altering the phenotype of a bird using avian somatic tissue-specific stem cells and do not require avian PGCs having an ES cell phenotype as claimed in the instant application.

The rejection of claims 44, 47, 48 and 51- 55 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 21-27 of copending Application No. 09/094176 has been withdrawn. The claims and specification of '176 did not teach isolating PGCs and stromal cells together from the genital ridge or gonad of an avian embryo.

7. Claims 44, 47, 48 and 51-55 remain rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 8-10 of U.S. Patent No. 5,340,740 in view of Chang (1995, Cell Biol. Internat'l., Vol. 19, page 143-9).

Claims 1 and 8-10 claim a sustained culture of undifferentiated avian cells having an ES cell phenotype and methods of making such a culture. '740 did not claim culturing the cells on avian feeder cells or the cell culture made by the method.

However, at the time of filing, Chang taught culturing PGCs on avian stromal cells. Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to isolate avian cells having an ES cell phenotype as taught by >740, wherein the avian cells are cultured on avian feeder cells. One of ordinary skill in the art at the time the invention was made would have been motivated to use avian feeder cells to increase the number of PGCs as taught by Chang (abstract).

Applicants' arguments on pg 31 are noted but do not specifically point to one limitation that is missing in the combined teachings of '740 and Chang. Applicants argue "it would not be possible to find such motivation as the understanding of the ordinary artisan at the time the application was filed was that PGCs isolated after stage 14 would be incapable of forming the claimed sustained culture." Applicants' argument is not persuasive because Chang taught culturing cells isolated from the genital ridge at Stage 27 for 5 days.

8. Claims 44, 47, 48 and 51-55 remain rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 5,656,479 or 5,830,510 in view of Chang (1995, Cell Biol. Internat'l., Vol. 19, page 143-9) for reasons of record.

Claim 1 of '479 and '510 are directed toward a sustained avian cell culture consisting essentially of undifferentiated avian cells expressing an embryonic cell phenotype. Claim 2 states the cells may be cultured on STO feeder cells in the presence of LIF. '479 and '510 did not claim culturing the cells on avian feeder cells.

However, at the time of filing, Chang taught culturing PGCs and stromal cells isolated together from the genital ridge of a stage 27 embryo on preconditioned, stage 27 avian feeder cells. Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to isolate avian cells having an ES cell phenotype as claimed in '479 and '510 wherein the avian cells are cultured on avian feeder cells. One of ordinary skill in the art at the time the invention was made would have been motivated to use avian feeder cells to increase the number of PGCs as taught by Chang (abstract).

Applicants' arguments on pg 32 are noted but do not specifically point to one limitation that is missing in the combined teachings of '740 or '510 and Chang. Motivation to combine the references has been provided. The art does not teach away from the invention because Chang taught culturing cells isolated from the genital ridge at Stage 27 for 5 days. A culture sustained for 5 or 14 days is not structurally or functionally different than a culture sustained for one or two months as claimed.

8. Claims 44, 47, 48 and 51-55 remain rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-12 of U.S.

Patent No. 6,156,659 in view of Chang (1995, Cell Biol. International., Vol. 19, page 143-9) for reasons of record.

Claims 1-12 of '659 claim a method of culturing undifferentiated avian cells having an ES cell phenotype for at least 14 days using LIF, bFGF, IGF and SCF. '659 did not claim culturing the cells on avian feeder cells.

However, at the time of filing, Chang taught culturing PGCs on avian stromal cells isolated from the genital ridge of Stage 27-28 embryos. Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to isolate avian cells having an ES cell phenotype as taught by '659, wherein the avian cells are cultured on avian feeder cells. One of ordinary skill in the art at the time the invention was made would have been motivated to use avian feeder cells to increase the number of PGCs as taught by Chang (abstract).

Applicants' arguments on pg 33 are noted but do not specifically point to one limitation that is missing in the combined teachings of '659 and Chang. Motivation to combine the references has been provided. The art does not teach away from the invention because Chang taught culturing cells isolated from the genital ridge at Stage 27 for 5 days. A culture sustained for 14 days as in '659 is not structurally or functionally different than a culture sustained for one or two months as claimed.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Wilson who can normally be reached on Monday through Friday from 9:00 am to 5:30 pm at 571-272-0738.

Questions of a general nature relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-1235.

If attempts to reach the examiner, patent analyst or Group receptionist are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached on 571-272-0804.

The official fax number for this Group is (703) 872-9306.

Michael C. Wilson

MICHAEL WILSON
PRIMARY EXAMINER